REMARKS

Justification for the amendments is as follows. Claims 1, 10, and 11 are amended to recite that the HIF prolyl hydroxylase inhibitor increases expression of the gene encoding γ-globin in a cell selected from the group consisting of hematopoietic stem cells and blast-forming unit erythroid (BFU-E) cells, support for which can be found throughout the specification, e.g., at paragraph [0028] and in original claim 27.

Claims 2-5 are canceled herein without prejudice to their renewal. Applicants specifically reserve the right to prosecute the subject matter of the canceled claims in continuing or divisional applications.

No new matter is introduced by any of these amendments, and entry of the amendments is respectfully requested.

I. Claim Status

Claims 1-47 were originally filed and were subject to restriction. Applicants elected Group 1, claims 1-36 and 39-45, for prosecution. In an amendment filed 5 September 2008, Applicants amended claims 1-3, 9-11, 16, 19, 21, 22 and 28, added new claims 48 and 49, and canceled claims 6-8 and 39-45 without prejudice to their renewal. The Examiner has withdrawn claims 17, 18, 34, 35, 46 and 47 from consideration based on election of species for examination. Thus, claims 1-5, 9-16, 19-33, 36, 48 and 49 are the subject of the present action. Applicants have herein amended claims 1, 10, and 11, and canceled claims 2-5 without prejudice.

II. Rejections Withdrawn

Applicants appreciate reconsideration and withdrawal of all rejections made in the previous Office Action.

III. New Rejections

A. Double Patenting

The Examiner provisionally rejected claims 1-5, 9, 10, 11-16, 19-21, and 23-27 under 35 U.S.C. §101 as claiming the same invention as that of claims 1-9, 10, 11-16, 17-24, and 34-56 of co-pending Application No. 11/348,294.

In accordance with section 804(I)(B)(2) of the Manual of Patent Examining Procedure (Eighth Edition, Revised July 2008), Applicants hereby request that this provisional statutory double patenting rejection be held in abeyance until this is the only rejection remaining in the subject application.

B. Rejections under 35 U.S.C. §102

1. The Examiner rejected claims 1-5, 9-16, 19, 21-25, and 48-49 under 35 U.S.C. §102(e) as being anticipated by Klaus et al., U.S. Patent Application Publication No. 2003/0153503 (Klaus et al.), as evidenced by Pace et al. (2000, Experimental Hematology 28:283-293) (Pace et al.). As claims 2-5 are canceled above, the rejection is moot as it applies to these claims.

The Examiner stated "Klaus teaches a method for increasing endogenous erythropoietin in vitro and in vivo comprising administering a compound that inhibits HIF prolyl hydroxylase enzyme activity ... which

increases endogenous erythropoietin ..." and "[e]rythropoietin increases expression of the gene encoding gamma globin thus increasing the level of fetal hemoglobin as evidenced by Pace et al." (Office Action, page 10.)

Independent claims 1, 10, and 11 as amended above recite that the HIF prolyl hydroxylase inhibitor "increases expression of the gene encoding γ-globin in a cell selected from the group consisting of hematopoietic stem cells and blast-forming unit erythroid (BFU-E) cells." Neither Klaus et al. nor Pace et al. discloses "administering ... a HIF prolyl hydroxylase inhibitor which increases expression of a gene encoding γ-globin in a cell selected from the group consisting of hematopoietic stem cells and blast-forming unit erythroid (BFU-E) cells" as recited in the claims as amended above. Thus, Klaus et al., read alone or as evidenced by Pace et al., fails to anticipate claims 1, 10, and 11, or dependent claims 9, 12-15, 19, 21-25, and 48-49.

Independent claim 16 recites "[a] method for increasing the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by a cell or population of cells, the method comprising administering to the cell or population of cells a hypoxia-inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding γ-globin." Neither Klaus et al. nor Pace et al. disclose that a HIF prolyl hydroxylase inhibitor would "increase expression of the gene encoding γ-globin" in a cell or population of cells. Thus, Klaus et al., read alone or as evidenced by Pace et al., fails to anticipate claim 16.

In summary, claims 2-5 are canceled above and Klaus et al. fails to anticipate amended claims 1, 9-16, 19, 21-25, and 48-49; thus, Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §102(e) as being anticipated by Klaus et al., as evidenced by Pace et al.

C. Rejections under 35 U.S.C. §103

1. The Examiner rejected claims 1-5, 9-16, 19, 20, 21-25, and 48-49 under 35 U.S.C. 103(a) as being unpatentable over Klaus et al., Pace et al., and Tung et al., International Publication No. WO 97/12855 (Tung et al.). As claims 2-5 are canceled above, the rejection is moot as it applies to these claims.

The test for non-obviousness articulated by the Court of Appeals for the Federal Circuit in *In re Vaeck* requires consideration of at least the following factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should practice the claimed invention; and (2) whether the prior art would also have provided a reasonable expectation of success to such a skilled artisan. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The first requirement goes to the question of motivation, and refers to a line of well established cases that there must be some logical reason at the time of the invention for modifying the cited references along the lines of the invention; otherwise the use of the teachings as evidence of non-obviousness will entail prohibited hindsight. *Ex parte Stauber and Eberle*, 208 USPQ 945 (Bd. App. 1980). For at least the reasons presented below, Applicants submit that claims 1, 9-16, 19-25, and 48-49 as amended above are non-obvious in view of Klaus et al., Pace et al., and Tung et al., singly or in combination.

Independent claims 1, 10, and 11 are amended above to recite that the HIF prolyl hydroxylase inhibitor "increases expression of the gene encoding γ-globin in a cell selected from the group consisting of hematopoietic stem cells and blast-forming unit erythroid (BFU-E) cells." None of Klaus et al., nor Pace et al., nor Tung et al. teaches or suggests "administering ... a HIF prolyl hydroxylase inhibitor which increases expression of a gene encoding γ-globin in a cell selected from the group consisting of hematopoietic stem cells and blast-forming unit erythroid (BFU-E) cells" as recited in the claims as amended above. Further, no logical reason for modifying Klaus et al., Pace et al., and Tung et al. along the lines of the present invention is provided. Thus, claims 1, 10, and 11, and dependent claims 9, 12-15, 19-25, and 48-49 are non-obvious in view of any of Klaus et al., Pace et al., or Tung et al., singly or in combination.

Independent claim 16 recites "[a] method for increasing the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by a cell or population of cells, the method comprising administering to the cell or population of cells a hypoxia-inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding γ-globin." None of Klaus et al., nor Pace et al., nor Tung et al. teaches or suggests that a HIF prolyl hydroxylase inhibitor would "increase expression of a gene encoding

γ-globin" in a cell or population of cells. Thus, claim 16 is non-obvious in view of any of Klaus et al., Pace et al., and Tung et al., singly or in combination.

In summary, claims 2-5 are canceled above and Klaus et al., Pace et al., and Tung et al., each taken alone or in combination, fail to teach or suggest the invention of amended claims 1, 9-16, 19, 20, 21-25, and 48-49; thus, Applicants respectfully request that the rejection of these claims under 35 U.S.C. 103(a) as being unpatentable in view of these references be withdrawn.

2. The Examiner rejected claims 1-5, 9-16, 19, 21-33, 36 and 48-49 under 35 U.S.C. 103(a) as being unpatentable over Klaus et al., Pace et al., and Bohmer et al., International Publication No. WO 01/12784 (Bohmer et al.). As claims 2-5 are canceled above, the rejection is moot as it applies to these claims. For at least the reasons presented below, Applicants submit that claims 1, 9-16, 19, 21-33, 36, and 48-49 as amended above are non-obvious in view of Klaus et al., Pace et al., and Bohmer et al., singly or in combination.

Independent claims 1, 10, and 11 are amended above to recite that the HIF prolyl hydroxylase inhibitor "increases expression of the gene encoding γ-globin in a cell selected from the group consisting of hematopoietic stem cells and blast-forming unit erythroid (BFU-E) cells." None of Klaus et al., nor Pace et al., nor Bohmer et al. teaches or suggests "administering ... a HIF prolyl hydroxylase inhibitor which increases expression of a gene encoding γ-globin in a cell selected from the group consisting of hematopoietic stem cells and blast-forming unit erythroid (BFU-E) cells" as recited in the claims as amended above. Further, no logical reason for modifying Klaus et al., Pace et al., and Bohmer et al. along the lines of the present invention is provided. Thus, claims 1, 10, and 11 and dependent claims 9, 12-15, 19, 21-27 and 48-49 are non-obvious in view of any of Klaus et al., Pace et al., or Bohmer et al., singly or in combination.

Independent claim 16 recites "[a] method for increasing the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by a cell or population of cells, the method comprising administering to the cell or population of cells a hypoxia-inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding γ-globin." None of Klaus et al., nor Pace et al., nor Bohmer et al. teaches or suggests that a HIF prolyl hydroxylase inhibitor would "increase expression of a gene encoding γ-globin" in a cell or population of cells. Thus, claim 16 is non-obvious in view of any of Klaus et al., Pace et al., and Bohmer et al., singly or in combination.

Independent claim 28 recites "[a] method for increasing the level of fetal hemoglobin in a subject, the method comprising (a) administering to a population of cells a hypoxia-inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding γ-globin; and (b) transfusing the γ-globin expressing cells into the subject. None of Klaus et al., nor Pace et al., nor Bohmer et al. teaches or suggests that a HIF prolyl hydroxylase inhibitor would "increase expression of a gene encoding γ-globin" in a population of cells. Thus, claim 28 and dependent claims 29-33 and 36 are non-obvious in view of Klaus et al., Pace et al., and Bohmer et al., singly or in combination.

In summary, claims 2-5 are canceled above, and Klaus et al., Pace et al., and Bohmer et al., each taken alone or in combination, fail to teach or suggest the invention of amended claims 1-5, 9-16, 19, 21-33, 36 and 48-49; thus, Applicants respectfully request that the rejection of these claims under 35 U.S.C. 103(a) as being unpatentable in view of these references be withdrawn.

CONCLUSION

In view of the foregoing, Applicants submit that the claims are fully in condition for allowance and request early notification to that effect.

Applicants claim small entity status under 37 C.F.R. 1.27.

The Commissioner is hereby authorized to charge the total of the fees due in this communication to Deposit Account No. 50-0811, referencing Docket No. FP0617 US.

Please call Applicants' representative at 415-978-1745 with any questions regarding the present communication or the above-identified application.

Respectfully submitted,

Date: 6 July 2009 By: _____

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